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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/073,077	02/12/2002	Thomas R. Gadek	9491-058-27	3125

7590

04/07/2005

Supervisor, Patent Prosecution Services
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EXAMINER

COUNTS, GARY W

ART UNIT	PAPER NUMBER
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1641

DATE MAILED: 04/07/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

10/073,077

Applicant(s)

GADEK ET AL.

Examiner

Gary W. Counts

Art Unit

1641

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 19 January 2005.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-14 and 21-24 is/are pending in the application.
- 4a) Of the above claim(s) 21-24 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-14 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Status of the claims

The amendment filed January 19, 2005 is acknowledged and has been entered.

Election/Restrictions

1. Newly submitted claims 21-24 are directed to an invention that is independent or distinct from the invention originally claimed for the following reasons: Claims 21-24 require the step of detecting the non-covalent binding of the compound to the target by mass spectrometry and claims 1-14 do not require this limitation. Further, claims 1-14 require the step of screening the set of linked ligands to identify compound members that bind to the target and claims 21-24 do not require this limitation.

Since applicant has received an action on the merits for the originally presented invention, this invention has been constructively elected by original presentation for prosecution on the merits. Accordingly, claims 21-24 are withdrawn from consideration as being directed to a non-elected invention. See 37 CFR 1.142(b) and MPEP § 821.03.

Claim Rejections - 35 USC § 112

1. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

2. Claims 1-14 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 is vague and indefinite because the preamble of the claim does not correlate with the body of the claim. The preamble recites "a method of identifying compounds" whereas step (d) of the body recites "to identify compound members". Is applicant identifying a compound or is applicant identifying ligands of the compound or is applicant doing something else? Please clarify.

Claim 1 is vague and indefinite because it is unclear if the two members are linked together while bound to the target or does Applicant somehow cause the members to dissociate and recover the members and then chemically link the members or does Applicant somehow identify the two members bound to the target and then synthesize a molecule using members that correspond to the members that were bound to the target. Please clarify. As indicated by Applicant on page 21, lines 1-13, molecules from each set of target binding ligands are then selected and linked covalently to generate new linked ligands.

Claim 1 the recitation "member" is vague and indefinite. It is unclear if applicant is referring to the ligand or if applicant intends something else. Please clarify.

Claim 1 the recitation "members" is vague and indefinite. It is unclear if applicant is referring to the linked ligands or to something else. See also deficiencies found in claims 13 and 14. Please clarify.

Claim 2 the recitation "target binding ligands" is vague and indefinite because it is unclear if applicant is referring to the target binding ligands recited in claim 1 or if applicant is referring to other target binding ligands. See also deficiency found in claim 3. Please clarify.

Claim Rejections - 35 USC § 102

3. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

4. Claims 1 and 6-12 are rejected under 35 U.S.C. 102(b) as being anticipated by Shuker et al., (Discovering High-Affinity Ligands for Proteins: SAR by NMR, Science, Vol. 274, 29 November 1996)

Shuker et al disclose screening a first ligand that binds to a first binding site on a target and then optimizing the first ligand by creating analogs and screening the analogs to optimize binding. Shuker et al disclose screening for a second ligand that binds to a second binding site on a target and optimizing the second ligand by creating structurally related compounds and screening the structurally related compounds. Shuker et al disclose selecting two lead fragments and chemically linking the two lead fragments to produce a high-affinity ligand. Shuker et al disclose that the target can be a protein. Shuker et al disclose screening the linked ligands (compound). Shuker et al disclose the binding affinities of these five compounds for FKBP were measured in a fluorescence based assay (p. 1533). Shuker et al disclose that the linked compounds are selected from a large library composed of all combinations of the fragments (p. 1534).

Claim Rejections - 35 USC § 103

5. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

6. The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

7. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

8. Claims 2-4 are rejected under 35 U.S.C. 103(a) as being unpatentable over Shuker et al in view of Crooke et al (US 2002/0102572).

See above for teachings of Shuker et al.

Shuker et al differ from the instant invention in failing to teach the assembling step of (a) or (b) comprises measuring non-covalent binding of target binding ligands to the target by mass spectroscopy.

Crooke et al discloses methods to determine the dissociation constant of ligands that bind to biopolymer targets (p. 3). Crooke et al disclose that mass spectrometry provides for the determination of specificity and affinity of ligands and provides high throughput screening methods to analyze the specificity and affinity of ligands to molecular interaction sites. Crooke et al also discloses that mass spectrometry provides for the determination of exact chemical composition of affinity selected ligands originating from a combinatorial library and to determine the relative dissociation constants of ligands complexed to the target(paragraph 0129). Crooke et al discloses that the mass spectrometry provides for advances over known techniques such as NMR (method used by Shuker et al) (paragraphs 0004-0014).

It would have been obvious to one of ordinary skill in the art to incorporate mass spectrometry such as taught by Crooke et al into the method of Shuker et al because Crooke et al teaches that mass spectrometry provides for the determination of specificity and affinity of ligands and provides high throughput screening methods to analyze the specificity and affinity of ligands to molecular interaction sites. Crooke et al also discloses that mass spectrometry provides for the determination of exact chemical composition of affinity selected ligands originating from a combinatorial library and to determine the relative dissociation constants of ligands complexed to the target. Crooke et al further discloses that the mass spectrometry provides for advances over

known techniques such as NMR. Therefore one of ordinary skill in the art would have a reasonable expectation of success incorporating mass spectrometry such as taught by Crooke et al into the method of Shuker et a.

9. Claim 5 is rejected under 35 U.S.C. 103(a) as being unpatentable over Shuker et al in view of Wells et al (WO 00/00823).

See above for teachings of Shuker et al.

Shuker et al differ from the instant invention in failing to teach the first binding site is the same as the second binding site.

Wells et al disclose two ligands linked together to bind to two binding sites on a target biomolecule (p. 22). Wells et al disclose that these ligands have non-covalent affinity for the site of interest (p. 15). Wells et al disclose that linked ligands can bind to the target biomolecule comprising two binding sites that are the same. Wells e al disclose that each member of the linked conjugate can be from the same class.

It would have been obvious to one of ordinary skill in the art use linked ligands comprising ligands from the same class to bind to two sites on a target biomolecule that are the same because Wells et al shows that target biomolecules comprise two sites that are the same and Wells et al shows that using ligands from the same class allows for linked ligands that have non-covalent affinity for the site of interest and thus allows for new small drug leads (p. 3).

Allowable Subject Matter

10. Claims 13 and 14 would be allowable if rewritten to overcome the rejection(s) under 35 U.S.C. 112, 2nd paragraph, set forth in this Office action and to include all of the limitations of the base claim and any intervening claims.

The following is a statement of reasons for the indication of allowable subject matter: the prior art of record fails to teach or suggest a third set and fourth set where members of each of the third set and the fourth set compete with members of the first set for binding to the first binding site, but members of the third set do not compete with members of the fourth set for binding to the target.

Conclusion

11. No claims are allowed.

12. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure.

Sem et al., (US 2002/0028468) disclose methods for rapidly identifying drug candidates that can bind to an enzyme at both a common ligand site and a specificity ligand site.

Mammen (US 6,656,694) disclose a method for identifying a ligand for a second binding site on a biological substrate.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Gary W. Counts whose telephone number is (571) 2720817. The examiner can normally be reached on M-F 8:00 - 4:30.


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If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long Le can be reached on (571) 272-0823. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).



Gary Counts
Examiner
Art Unit 1641
March 24, 2005



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04/01/05